Remarks

Status of The Claims

Claims 2-5, 12-23, 25-28, and 30-34 are canceled.

Claims 1, 10, and 14 are currently amended.

Claims 1, 6-11, 14, 24, and 29 are currently pending in this application. Claim 1 is amended to pertain to a method to avoid silencing of a transgene comprising SEQ ID NO:16 operably linked to a polynucleotide encoding a chloroplast transit peptide. No new matter is added by the claim amendments.

Applicant wishes to thank the Examiner for his time and suggestions during the telephone conference of June 5, 2009. It is the understanding of the undersigned that the Examiner will issue an interview summary regarding the rejections of claims 10, 11, and 14.

Response To Claim Rejections Under 35 U.S.C. § 112 (Indefinite)

The Examiner rejects claims 1, 20, 11, 14, and 29 under 35 U.S.C. § 112, second paragraph, as allegedly being incomplete for omitting essential elements, i.e., a chloroplast transit peptide. According to the Examiner, the known polynucleotide "must encode a chloroplast transit peptide, operably linked to the nucleotide sequence encoding SEQ ID NO:15, as the chloroplast is where it exerts its functional activity."

Regarding claim 1:

Applicant submits that, in view of the current amendment to claim 1, this rejection is obviated. The current amendment positively cites a chloroplast transit peptide.

Regarding claim 10 and dependent claims 11 and 29:

Applicant respectfully disagrees with the Examiner. As discussed during the June 5, 2009 telephone conference between the Examiner and the undersigned, the rejection of claim 10 as indefinite for lacking a CTP is unwarranted. Claim 10 pertains to a plant cell comprising at least two polynucleotides, wherein said two polynucleotides encode the ***same*** polypeptide and wherein at least one of the polynucleotides is SEQ ID NO:18 operably to linked to a polynucleotide encoding a chloroplast transit peptide. It is clear that both polynucleotides encode a CTP; otherwise, they will not encode the same polypeptide. Claims 11 and 29 depend on claim 10; thus, the rejection of claims 11 and 29 is also unwarranted for the same reasons outlined, *supra*.

Regarding claim 14:

Also discussed and agreed upon during the conference of June 5, 2009 is that the rejection of claim 14 as indefinite for lacking a CTP is erroneous. It is the understanding of the undersigned that the Examiner will issue an interview summary stating the same.

Claim 14 is also rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which Applicant regards as the invention. According to the Examiner, there is "insufficient antecedent basis for the limitation, 'said artificial polynucleotide molecule.'" In response, Applicant amends claim 14 to read "an artificial polynucleotide," in lieu of "said artificial polynucleotide."

In view of the current amendments and arguments stated above, Applicant respectfully requests that the rejection of claims 1, 10, 11, 14, and 29 under 35 U.S.C. § 112 as indefinite be withdrawn.

Response To Claim Rejections Under 35 U.S.C. § 112 (Enablement)

Claims 1, 10, 11, and 29 remain rejected under 35 U.S.C. § 112, first paragraph, as failing to comply with the enablement requirement because, first, the claims "do not recite the level of divergence between the known and artificial polynucleotides, and therefore encompass artificial and known polynucleotides that are not sufficiently divergent to avoid transgene silencing," AND second, because the claims do not indicate that the essential element of a chloroplast transit peptide is also operably linked to the known polynucleotide. In response, Applicant herewith amends claim 1 to delete the word "divergent." Regarding claim 10 and dependent claims 11 and 29, Applicant submits that, as discussed with the Examiner in the June 5, 2009 telephone conference, this rejection is unwarranted because **both** the known and the artificial polynucleotides of claim 10 (and dependent claims 11 and 29) **encode a chloroplast transit peptide fused to an EPSPS sequence;** otherwise, they will not be encoding the same polypeptide.

Response To Claim Rejections Under 35 U.S.C. § 103

The Examiner rejects claims 1, 6-11, 14, 29, and 29 under 35 U.S.C. § 103(a) as obvious in view of Drake *et al.* (WO 97/46690) [December 11, 1997, Caroline R. Drake, *et al.*, Enhancement of gene expression], in combination with Barry *et al.* [U.S. Patent No. 5,633,435, issued May 27, 1997, Gerard F. Barry, *et al.*] and Murray *et al.* [Elizabeth E. Murray, *et al.*, Codon usage in plant genes, *Nucleic Acids Research* 17(2):477:498 (1989)]. According to the Examiner, these references in combination would allegedly result in the artificial polynucleotide encompassed by the claims.

Applicant respectfully disagrees with the Examiner. The currently pending claims pertain to methods, cells, and plants comprising the artificial sequence **SEQ ID NO:18** which is **not** obvious in view of the **combination** of the above-identified references. Furthermore, a prior art reference needs to be enabling, i.e., it must enable one of ordinary skill in the art to make the invention without undue experimentation. *See Impax Laboratories, Inc. v. Aventis Pharmaceuticals, Inc.*, 545 F.3d 1312, 88 U.S.P.Q.2d 1381 (Fed. Cir. 2008); *Monsanto Company v. Syngenta Seeds, Inc.*, 503 F.3d 1352, 84 U.S.P.Q.2d 1705 (Fed. Cir. 2007), *reh'g & reh'g en banc denied*, Jan. 17, 2008; *Amgen Inc. v. Hoechst Marion Roussel, Inc.*, 457 F.3d 1293, 79 U.S.P.Q.2d 1705 (Fed. Cir. 2006); *In Re Hoeksema*, 399 F.2d 269, 158 U.S.P.Q. 596 (C.C.P.A. 1968).

Applicant respectfully reminds the Examiner of the Examiner's prior statements regarding enablement. In his rejection of previously presented claims 1, 2-11, 13, 29, and 34, the Examiner stated in the office action of October 24, 2008 that "the claims [were] not limited to artificial and known polynucleotides encoding EPSPS synthases, but broadly encompass any type of proteins." The Examiner argued that the Applicant's own specification "does not enable constructing artificial polynucleotides encoding proteins that differ in sequence identity from that encoded by the known or original polynucleotide, except for EPSPS" (p. 6). According to the Examiner, "no guidance [was] provided regarding what kind of amino acid changes can be sustained by any given protein without affecting its functional activity." The Examiner proceeds to explain that the "**example of EPSPS is not applicable to any other type of protein**, as other proteins of course have differing structures and mechanisms of actions." The Examiner further argues that the "type of number of changes any protein can sustain, if at all, *cannot be extrapolated* to any other protein" [emphasis added] and that "in the absence of further guidance,

undue experimentation would be required for one skilled in the art to determine how any given protein may be changed without affecting its functional activity."

Along the same lines, Drake *et al.* is, therefore, **not** a reference that enables claims directed to methods, plants, and cells comprising polynucleotides other than the native tomato phytoene synthase gene, TOM5. Drake *et al.* does not enable bacterial genes or EPSPS synthase genes such as SEQ ID NO:18. Drake *et al.* is limited in its scope because it only: **first**, teaches a single gene from tomato and its modification; **second**, teaches a native plant gene (not a bacterial transgene); and **third**, provides meager guidance on how to create artificial genes. Drake *et al.* does not teach how to create artificial genes besides the general five steps outlined on page 4. Drake *et al.* reads:

> To obtain the gene for insertion in accordance with this invention it may be necessary to synthesize it. The general parameters within which the nucleotide sequence of the synthetic gene compared with the gene already present may be selected are:
>
> 1. Minimise the nucleotide sequence similarity between the synthetic gene and the gene already present in the plant genome;
>
> 2. Maintain the identity of the protein encoded by the coding region;
>
> 3. Maintain approximately the optimum codon usage indicated for the target genome;
>
> 4. Maintain approximately the same ratio of purine to pyrimidine bases; and
>
> 5. Change the promoter or, at least, the 5'-intervening region.

These general guidelines do not enable proper expression of any artificial gene. In contrast, Applicant teaches several examples of artificial EPSPS and phosphinothricin acetyltransferase polynucleotides that are divergent from their respective native or wildtype genes in that they share no lengths of polynucleotide sequence greater than 23 nucleotides that are identical (*see* Applicant's specification, p. 14, ll. 10-18). Applicant also teaches "replacing at

least one of every eight contiguous codons with a different codon selected from the codon usage table and adjusting the percent codon usage for each amino acid encoded by the polynucleotide to substantially the same percent codon usage found in the codon usage table." Furthermore, Applicant teaches that "[a]dditional steps can include introducing a translational stop codon in the second and third open reading frame of the new polynucleotide sequence; eliminating some translational start codons in the second and third open reading frames; adjusting local GC:AT ratio to about 2:1 over a range of about 50 nucleteotides; disrupting potential polyadenylation signals or potential intron splice sites; removing at least one restriction enzyme site of six contiguous nucleotides or greater; and comparing the sequence identity of the new artificial polynucleotide to an existing polynucleotide that encodes the same or similar protein so that the sequence identity between the two polynucleotides is not more than 85 percent." *See* Applicant's specification, p. 30, ll. 6-19.

Therefore, Applicant submits that Drake *et al.* is not enabling prior art reference and is very limiting in scope.

In view of the current claim amendments and the above arguments, Applicant respectfully requests that the rejection of the claims under 35 U.S.C. § 103(a) be withdrawn and the application proceed to allowance.

Fees

The response is timely filed; thus, no fees are believed to be due at this time. The response is also filed within two months of the mailing date of the final office action of April 20, 2009. As the two-month date falls on Saturday, June 20, 2009, filing the response on Monday, June 22, 2009, is considered to be within two months of the mailing date of the final action.

However, should any additional fees under 37 C.F.R. §§ 1.16-1.21 be required for any reason relating to the enclosed materials, the Commissioner is hereby authorized to deduct any additional fees from Howrey LLP Deposit Account 08-3038/11899.0235.PCUS00.

Respectfully submitted,

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